Royal College of Physicians
11 St Andrews Place
Regent's Park
London NW1 4LE
Tel: +44 (0)20 3075 1560

www.rcplondon.ac.uk

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Re: Lapatinib or trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone-receptor-positive breast cancer that overexpresses HER2

I write on behalf of the NCRI/RCP/RCR/ACP/JCCO who collaborate when responding to NICE oncological consultations. We are grateful for the opportunity to comment on the above ACD and would like to make the following comments.

The conclusions of the ACD seem to be reasonable in so far as they go but will be disappointing to patients with metastatic breast cancer and to clinicians who treat them.

The most fundamental issue in the appraisal is that no comparison was performed in the cost-effectiveness of anti-HER2 therapy combined with an aromatase inhibitor with trastuzumab in combination with chemotherapy or even with trastuzumab monotherapy. Both of these therapeutic options have previously been recommended by NICE for women with HER2 positive metastatic breast cancer (although in rather restricted circumstances for trastuzumab monotherapy). In current clinical practise these options are the only way in which anti-HER2 therapy can be delivered to this patient group. For the population considered in the appraisal, if patients wish to avoid chemotherapy or clinicians are reluctant to give chemotherapy then the options for the majority are either initial treatment with an aromatase inhibitor as monotherapy or reluctant acceptance of chemotherapy and trastuzumab. Those who are treated initially with endocrine therapy, which the randomised evidence considered by the NICE committee clearly shows is inferior to AI and anti-HER2 combination therapy, will be forced into a decision about chemotherapy as a means to obtain anti-HER2 therapy at the point of failure of endocrine therapy. There is no trial data comparing endocrine therapy in combination with anti-HER2 therapy, either alone or in combination with chemotherapy which makes a comparison of efficacy very difficult but this is the real world decision facing patients and clinicians. Availability of anti-HER2 therapy in combination with an AI is a suitable treatment for those few patients for whom chemotherapy is not an option.

The recent dramatic price fall in the cost of anastrozole and letrozole as these drugs have come off patent will affect the economic assessments performed for the Committee although probably not to a significant degree. They would however significantly affect any comparison between antiHER2 therapy and AI's with chemotherapy and trastuzumab.

The Committee commented that the TAnDEM and EGF100151 trials showed a very uncertain overall survival gain. The trial data however is clearly skewed by crossover of patients in the TAnDEM trial to trastuzumab post-progression. This is also likely but undocumented for those enrolled in EGF100151.

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